

REMARKS

Continued Examination Under 37 CFR 1.114:

Section 1. Applicants' request for continued examination under 37. CFR 1.114, filed 17 July 2003, has been acknowledged and entered. The finality of the previous office action was withdrawn.

Allowable Subject Matter:

Sections 11 and 12. Applicants note that Claims 10, 12, 14, and 20, drawn to plasmids, expression cassettes, and transformed microorganisms, and Claim 47, drawn to an isolated nucleic acid fragment, are allowed.

Patentability Under 35 U.S.C. § 102:

Sections 5, 6, and 13.

Claims 1-2, 9, 11, 13, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi *et al.* (*Biochemistry* (1992) 31:9000-9007). The Examiner states in Section 13, pages 11 and 12, that:

"In order to anticipate the claims, Kobayashi must teach that the sequence does two things. Kobayashi must teach that the sequence encodes a nitrilase (see page 9004, figure 3). Second Kobayashi must teach a sequence which would hybridize under the conditions stated to SEQ ID NO:5."

The Examiner observes in Section 6 of the office action that Kobayashi *et al.* disclose an isolated nucleic acid sequence fragment that encodes a nitrilase enzyme, which sequence:

- i) would hybridize to SEQ ID NO:5 under the stated conditions,
- ii) encompasses the completely complementary strand; and
- iii) is 71.274% identical to SEQ ID NO:5.

The Examiner also observes that Kobayashi *et al.* disclose expression of the nitrilase in an *E. coli* host cell using suitable regulatory sequences.

Reply:

Claim 1 has been amended to recite highly stringent conditions. Support for this amendment is found in the specification as filed on page 24, at lines 17-19. Additionally, one of skill in the art can determine the hybridization specificity based on the melting temperature (T_m) of the nucleic acid sequence. Support for calculating the T_m of the respective sequences is found starting on page 24, line 20 and concluding on page 25, line 13.

The Kobayashi *et al.* disclosure does not teach a nitrilase sequence that would hybridize under highly stringent conditions to a nucleic acid fragment encoding SEQ ID NO:5

with which it shared only 71 % identity. The second requirement to find anticipation is not satisfied.

As shown above, the disclosure of Kobayashi *et al.* does not anticipate the subject matter of amended Claim 1. Applicants request reconsideration of Claim 1 and related dependent claims, withdrawal of the rejection, and prompt allowance of the Claims.

Claim 2 has been amended to recite “at least 90% identity... compared to a polypeptide encoded by the sequence identified in SEQ ID NO:5”. The sequence disclosed in Kobayashi *et al.* (*Biochemistry* (1992) 31:9000-9007) shares only 71.274 % identity with Applicants’ disclosed sequence and therefore would not anticipate the subject matter claimed in amended Claim 2.

Amended independent Claims 1 and 2 are novel and not anticipated by Kobayashi *et al.* Rejections for anticipation of claims dependent upon Claims 1 and 2 (*i.e.*, Claims 9, 11, 13, and 15) are therefore also overcome.

Applicants respectfully request reconsideration of the rejected claims as amended, withdrawal of the rejections for anticipation, and prompt allowance of Claims 1-2 (as amended), 9, 11, 13, and 15.

With regard to the Examiner’s observations in section 13 at page 11 on Claim 5 (containing a limitation on the source of the nucleic acid), Applicants note that Claim 5 was cancelled in the Reply mailed 14 July 2003 and therefore is not currently pending.

**Patentability Under 35 U.S.C. §103:
Sections 7, 9, 10 and 13.**

Claims 16-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi *et al.* in view of Anderson *et al.* (U.S. Patent 5,935,840). Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi *et al.* in view of Anderson *et al.* (U.S. Patent 5,935,840), and further in view of Galen (U.S. Patent 6,413,768). The Examiner states that Kobayashi *et al.* teach the limitations of Claims 1-2, 9, 11, 13, and 15. The Examiner states that Anderson *et al.* teach the use of chromosomally integrated vectors and ribosome binding sites, and that Galen teaches the use of *E. coli* MG1655.

Reply:

Applicants have amended Claims 1 and 2 on which Claims 16-19 ultimately depend. For the reasons set out above, Kobayashi *et al.* do not teach or suggest the limitations of amended Claims 1-2, 9, 11, 13, and 15. In fact, this was also true with regard to the amended Claim 2 and New Claim 49 proposed in the Reply of July 2003 where the % identity was set at 80% and 90%, respectively. Without the disclosure of Kobayashi *et al.* to support the

findings of prima facie obviousness under U.S.C. 103(a) set out in Sections 9 and 10, the rejections for obviousness of dependent Claims 16-19 and of Claim 46 have been overcome.

In the event that the rebuttal arguments are deemed insufficient to overcome the *prima facie* case for obviousness, Applicants maintain that the claimed subject matter provides unexpected results and advantages not obtainable from Kobayashi *et al.* or from combining the teachings of the cited art. Applicants maintain that the composition of Kobayashi (the nucleic acid sequence that encodes for the *Rhodococcus rhodochrous* K22 nitrilase) and the compositions of amended Claims 2 and 49 (nucleic acid sequences that encode for variants of the *Acidovorax facilis* 72W nitrilase) are not the same. This position is supported by the fact that the nitrilase enzyme encoded by the gene sequence reported by Kobayashi *et al.* has markedly different enzyme activities and temperature stability as compared to the nitrilase enzymes encoded by the nucleic acid fragments claimed in the present application.

The unexpected results and advantages of the claimed subject matter (different substrate specificity, different thermal stability, different reactivity, etc.) were detailed in the Reply of July 2003 at pages 7 through 9 and are incorporated herein in their entirety.

Applicants respectfully request reconsideration of the rejected claims in light of the amendments and remarks entered, withdrawal of the rejections for obviousness, and prompt allowance of Claims 16-19 and 46.

Section 8.

Reply:

The Examiner correctly presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made.

Patentability Under 35 USC § 112:

Having shown that the claims under prosecution encompass novel and non-obvious subject matter, the only remaining issues are to matters of form under 35 U.S.C. 112.

Sections 2, 3, and 13 regarding 35 USC § 112, 1st paragraph:

Claims 2 and 49 stand rejected under the requirements of the first paragraph for lacking a sufficient written description of the claimed subject matter in the specification to convey that the inventor(s), at the time the application was filed, had possession of the claimed invention. In Section 3, the Examiner points to the USPTO written description 1999 guidelines and in Section 13 describes the issue set out in the Guidelines as “whether the structure plus the function is sufficient so that there is minimal variation among the species.” The Examiner concludes on page 10 that this expectation would not be met since the scope of the claim encompasses species with “significant variation”.

The Examiner is additionally of the opinion that the rejected claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The Examiner further states, beginning on page 4:

“In the current situation, the definition of the nitrilase gene using the hybridization language of paragraph (c) of claim 1 lack any specific required structure. Thus, these claims present precisely the situation of naming a type of material which is generally known to likely exist, but, except for the two specific nitrilase sequences given fails to provide descriptive support for these generic claims... [T]he current claims define the nitrilase nucleic acids solely by their functional utility, as fragments or components capable of hybridization to specific sequences, with any definition of particular gene of sequences claimed... In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which encode the nitrilase enzymes disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.”

Reply:

Claims 2 and 49 have been amended respectively to include sequences encoding a polypeptide with nitrilase activity and having at least 90 % and 95% identity to a polypeptide encoded by SEQ ID NO:5. Basis for the amendments can be found in the specification as filed on page 11, lines 18-27, and on page 26, lines 8-12. The procedures for making such variants of SEQ ID NO:5 are known to those of ordinary skill in the art and the specification describes an assay that will identify other proteins with the claimed enzymatic activity.

Applicants have provided generic embodiments: the novel nucleic acid sequence encoding SEQ ID NO:5, the deposit of biological material from which the sequence was determined, and variants of that nucleic acid sequence encoding SEQ ID NO:5 having certain common attributes. The claimed subject matter does not have “significant variation” since all of the variants must possess the specified enzymatic activity and must have at least 90 or 95% identity to the reference sequence, SEQ ID NO:5. The species disclosed is representative of the genus because all members have at least 90 or 95 % identity with the reference compound and because Applicants provided an assay to identify all of the at least 90 or 95% identical variants of SEQ ID NO:5 that are capable of the required enzymatic activity.

Thus, Applicants maintain that they were in possession of the necessary common attributes possessed by the members of the genus. This analysis is supported in the Guidelines set forth by the US Patent and Trademark Office (*Guidelines for Examination of Patent Applications Under the 35 USC 112, 1, “Written Description” Requirement*, 66 Fed Reg. 1099, 1106 (Jan 5, 2001)). The Guidelines provide that written description requirements for a claim drawn to a genus can be satisfied by sufficient description of a representative

number of species by actual reduction to practice ,...or by disclosure of relevant identifying characteristics.

“Relevant identifying characteristics” may include structure or other physical and /or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show that the applicant was in possession of the claimed genus. (See MPEP 2100-168, Rev. 1, February 2003, citing *The Regents of the University of California v. Eli Lilly and Co.*, 119 F3d at 1568, 43 USPQ2d 1398 at 1406 (Fed. Cir. 1997).)

In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 323 F3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002), the CAFC again endorsed that functional descriptions of genetic material can, in some cases, meet the written description requirement if those functional characteristics are “coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” 323 F.3d at 964 (quoting from the PTO’s Guidelines for ... “Written Description” Requirement, (2001 *supra*).

Applicants rely on the Examiner’s “Response to Arguments” at page 10, section 13, that the rejection under 35 USC § 112, 1st paragraph is “only maintained against the claims which recite percent identity.” Claim 1 does not recite percent identity. Therefore, Claim 1 is not rejected under this section of the patent statute although the Office Action addresses Claim 1.

Claims 2 and 49 do recite per cent identity and Applicants have addressed the related portions of the Office Action. However, reasons for the rejection of Claims 2 and 49 as set out above also include that the claimed material is “capable of hybridization to specific sequences”. Amended Claims 2 and 49 do not use this hybridization language to define the claimed material.

Applicants respectfully request reconsideration of amended Claims 2 and 49, withdrawal of the rejection, and prompt allowance of the application.

Sections 4 and 13 regarding 35 USC § 112, 2nd paragraph:

Claims 2 and 49 are further rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In maintaining this rejection, the Examiner states that

“the default values of the algorithm used to determine the % identity of the sequences encompassed by the claims need to be stated in the claim.”

Further, a caution is made that the default values must have basis in the specification or would be found to be prohibited as new matter.

Reply:

Applicants traverse this rejection. There is no blanket requirement in the statute or the rules that default values must be stated in the claims to provide sufficient definiteness under 35 USC § 112, 2nd paragraph. Support for the specific % identity (at 80, 90 and 95 % identify) with regard to SEQ ID NO:5 is found at page 11, lines 18-27. Support for the version of the software used to determine the % identity and the default values contained in the software are explicitly set out at page 26, lines 6-13, in the General Methods section related to the Examples. Applicants rely on that passage to fully support the amended Claims 2 and 49. There is no ambiguity in the specification about what default values are intended as no other default parameters are disclosed in the specification. That other default values may be used in software found on internet websites unrelated to Applicants' disclosure is irrelevant.

In light of the Remarks and amendments, Applicants respectfully request reconsideration of amended Claims 2 and 49, withdrawal of the rejection for lack of definiteness, and prompt allowance of the application.

In light of the Remarks and amendments proposed herein, reconsideration of Claims 1(as amended), 2(as amended), 9, 11, 13, 15-19, 46, and 49(as amended), withdrawal of the rejections, and the prompt allowance of the claims under prosecution are respectfully requested. Should any matter remain unresolved, please contact the undersigned.

Respectfully submitted,



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